

## REMARKS

### Status of the Claims

Claims 39-48, and 52-70 are currently pending. Claims 49 and 71-76 are withdrawn. Claims 52-61, and 63-70 are amended herein. Support for the amendments to the claims can be found throughout the specification, drawings, and original claims, for example, at least at page 11, Table 4 starting at page 67, and figure 18. The amendments do not represent new matter.

### References in the Specification to Internet Sites

Pursuant to MPEP § 608.01 VII, Applicant has amended the specification to make it certain that the text does not contain any hyperlinks or other forms of browser-executable code yet still reflect the information that was publicly available at or before the time of filing. Applicant appreciates that the content of a webpage can change over time or can disappear completely. With this in mind, Applicant memorialized the content of the websites cited in the specification by printing out the webpage on the date indicated in the specification (in some cases, the specification refers to the date in which the webpage was last updated).

Applicant submitted the website printouts in an Information Disclosure Statement (IDS) filed on January 10, 2001, the filing date of the application. A copy of the Form PTO-1449 that was submitted with the IDS was returned with the Office Action. The Examiner signed the form but would not consider the documents because the titles of the documents referred to a hyperlink. Applicant respectfully directs the Examiner's attention to MPEP § 608.01 VII which indicates that the requirement to delete embedded hyperlinks or other forms of browser-executed code does not apply to PTO-892 or PTO-1449 (PTO/SB/08). Moreover, the Office Action failed to provide any reasoning for not considering the content of the cited websites as embodied in the printouts. Applicant respectfully requests that the Examiner consider the printouts submitted in the IDS of January 10, 2001.

**Sequence Listing**

The Office Action acknowledges Applicant's "Sequence Listing" submission of November 4, 2004 but states that a resubmission is needed, referring to the problem report enclosed therewith. A sequence listing, however, was not filed by Applicant on November 4, 2004. Applicant mailed a Response to Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence disclosures on October 17, 2002. Moreover, the problem report appears to be directed to the originally-filed Sequence Listing rather than the Sequence Listing mailed on October 17, 2002 in Response to the Notice. The October 17, 2002 Sequence Listing includes <220> to <223> features to explain that the Xaa at positions 2, 3, 5, and 6 of SEQ ID NO:1 can be any amino acid. Applicant respectfully requests clarification as to whether a Sequence Listing must be resubmitted.

**The Rejections Under 35 U.S.C. § 112, First Paragraph****The Enablement Rejection**

The Office Action asserts that none of the pending claims are enabled by the specification. The rejection states that the scope of the claims is not commensurate with the enablement provided by the disclosure. Applicant respectfully disagrees. Using the specification as a guide, one of ordinary skill in the art could make and use a cell that produces a glycoconjugate of interest in the absence of an exogenously supplied nucleotide without undue experimentation, wherein the cell comprises heterologous genes encoding one or more sugar nucleotide regenerating enzyme and one or more glycosyltransferase.

Genes encoding enzymes involved in sugar-nucleotide generation and regeneration were known in the art at the time of filing (page 10, lines 14-16). In addition to this high level of skill in the art, the specification provides examples of combinations of enzymes that may be used to regenerate many sugar nucleotides including UDP-Gal (page 11, lines 3-9, and FIGS. 1, 3, 4, 5, and 15), UDP-Glc (page 11, lines 11-26, and FIGS. 6 and 18), UDP-GlcNAc (page 12, lines 5-26, and FIG. 7), UDP-GalNAc (page 13, line 2, to page 14, line 12, and FIG. 8), UDP-GlcA (page 14, line 14, to

page 15, line 14, and FIGS. 6, 9, and 19), CMP-NeuNAc (page 15, line 16, to page 17, line 4, and FIG. 10), GDP-Man (page 17, line 6, to page 18, line 4, and FIG. 12), GDP-Fuc (page 18, line 6, to page 20, line 19, and FIGS. 12 and 17).

As acknowledged in the Office Action (page 5 of Office Action) and as indicated in the specification (page 21, lines 13-18), glycosyltransferases and their properties were well known in the art at the time of filing. Moreover, the specification provides specific an extensive list of examples of glycosyltransferases that may be used based on their donor specificity (page 22, line 8, to page 26, line 4). Given this teaching and the level of understanding of recombinant expression in the art, one of skill in the art could express an enzyme having a particular glycosyltransferase activity in an organism without undue experimentation. One of skill in the art may recognize that certain eukaryotic glycosyltransferases may not be efficiently expressed in prokaryote cells and vice versa. As the specification describes, other expression systems, including yeast, insect cells, or mammalian cells, may be used instead. Moreover, because often there are eukaryotic and prokaryotic enzymes known in the art that have the same or similar glycosyltransferase activity, if one wished to use a prokaryotic expression system, one of skill in the art could choose to use the prokaryotic enzyme having the desired activity.

The Examples provide assays that can be used to test for the ability of the organism to recombinantly express a functional enzyme and to test for the ability of the enzymes to work together to produce the desired product, prior to constructing the superbug. One of skill in the art could screen for appropriate enzymes and combination of enzymes that function together in a certain system prior to going through the process of putting all the genes for the enzymes together to create a superbug. Thus, using the specification as a guide, the amount of experimentation needed by one of skill in the art to make and use the claimed invention would not be undue.

In addition to the extensive guidance given by the specification and the high level of skill in the art, the specification further provides several working examples of “superbugs.” Contrary to the assertions made in the rejection, the Examples describe the construction and use of three different superbugs, not just one. Moreover, the enzymes used to produce the superbugs were not all of *E. coli* origin. For example, the superbug of Example 3 contained a sucrose synthase gene from *Anabaena sp.* (a cyanobacterium).

As further evidence of the feasibility of producing a superbug using the methods described in the specification, Applicant submits herewith in Appendix A post-filing publications by one or more of the present co-inventors describing creation and use of a superbug, including the creation of a yeast “superbug ” (Shao *et al.*).

Applicant respectfully requests withdrawal of the rejection of the claims for lack of enablement.

#### The Written Description Rejection

The specification is replete with examples of enzymes having given activities, enzymes that may be used together to regenerate sugar nucleotides, and figures providing diagrams of plasmids that are useful in creating the cells of the present claims, along with descriptions as how to create the plasmids. The sequence of thousands of sugar nucleotide regenerating enzymes, epimerases, and glycosyltransferases were known in the art at the time of filing. Moreover, the specification provides several working examples of cells of the present claim. A skilled artisan would recognize that at the time of filing the Applicant was in possession of the concept of a cell that produces a glycoconjugate of interest in the absence of an exogenously supplied nucleotide triphosphate and comprises heterologous genes encoding one or more sugar nucleotide regenerating enzyme and one or more glycosyltransferase. Applicant respectfully requests withdrawal of the rejection of the claims for lack of written description.

#### The Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 47 and 48 stand rejected for reciting “genes encoded within one or more plasmids.” The rejection contends that the claims are indefinite because it is the enzyme that is encoded by the gene. Applicant respectfully disagrees that one of skill in the art would limit the meaning of the term “encoded” in such a way. It was common in the art at the time of filing to refer to genes “encoded” by plasmids, *e.g.*, Singh and Sharma, “Detection of plasmid-encoded gusA gene in GUS-positive *Escherichia coli*,” Biotechniques 1999 Feb;26(2):261-4. Thus, use of the phrase “genes encoded within one or more plasmids” does not render the claim indefinite.


Claims 52-61, 63-65, and 67-70 stand rejected for containing one or more abbreviations. As amended herein, the claims no longer contain any abbreviations, rendering the rejection moot. Applicant reserves the right to pursue the subject matter of the previous claims in future prosecution.

### Conclusion

In light of the amendments and comments made herein, Applicant submits that the application is in condition of allowance and requests notification thereof. The Examiner is invited to call the undersigned to discuss any matter that may expedite allowance of this application.

Respectfully submitted,

Date: June 23, 2005



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